

09918687 072704
T07270 09918687

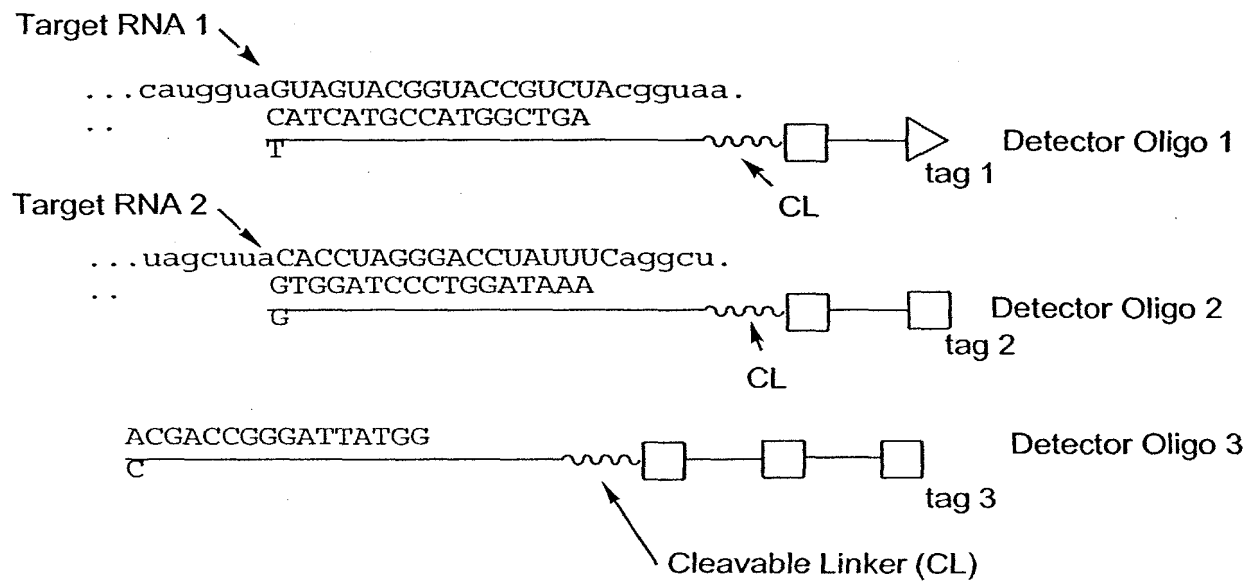


FIGURE 1

Cleave tags

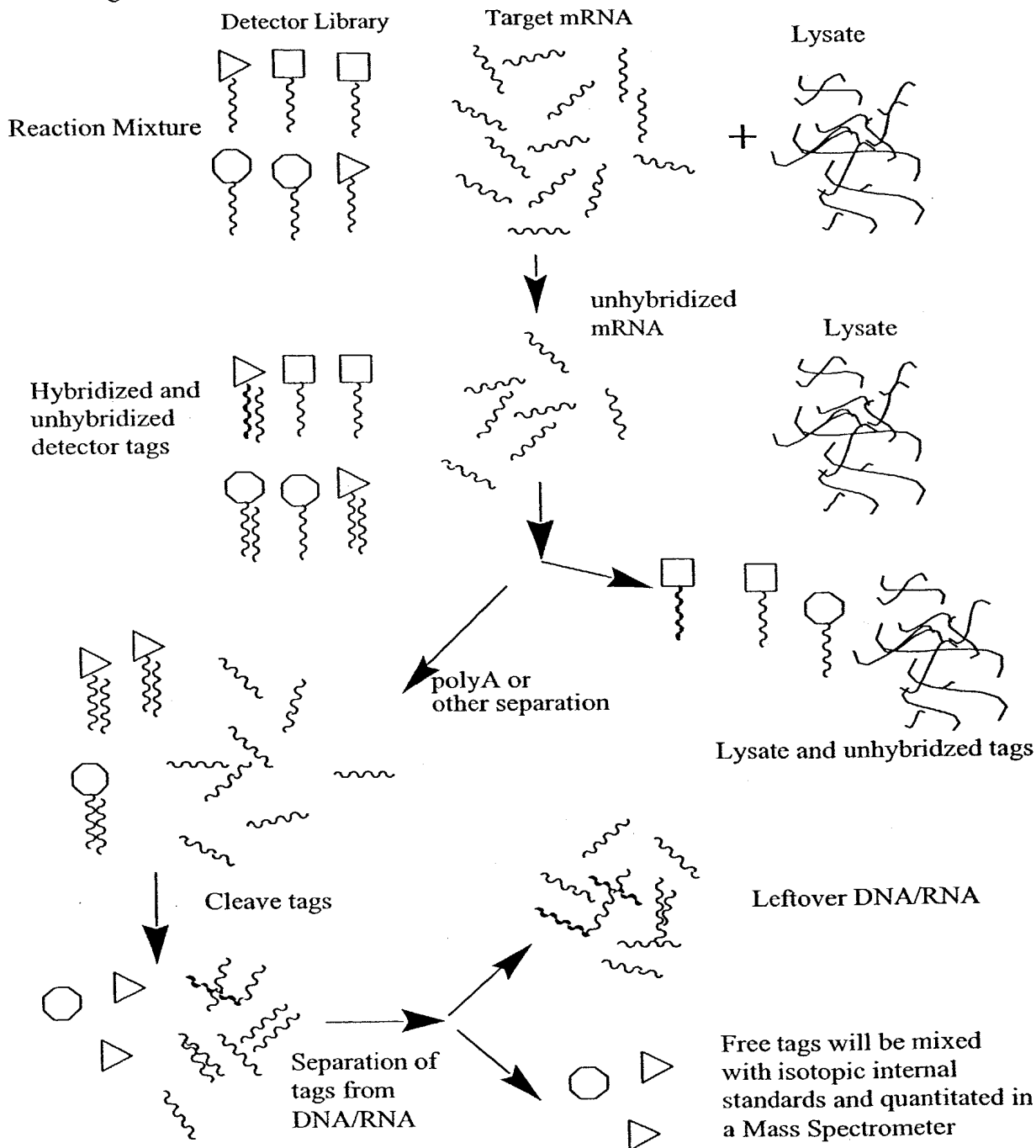


FIGURE 2

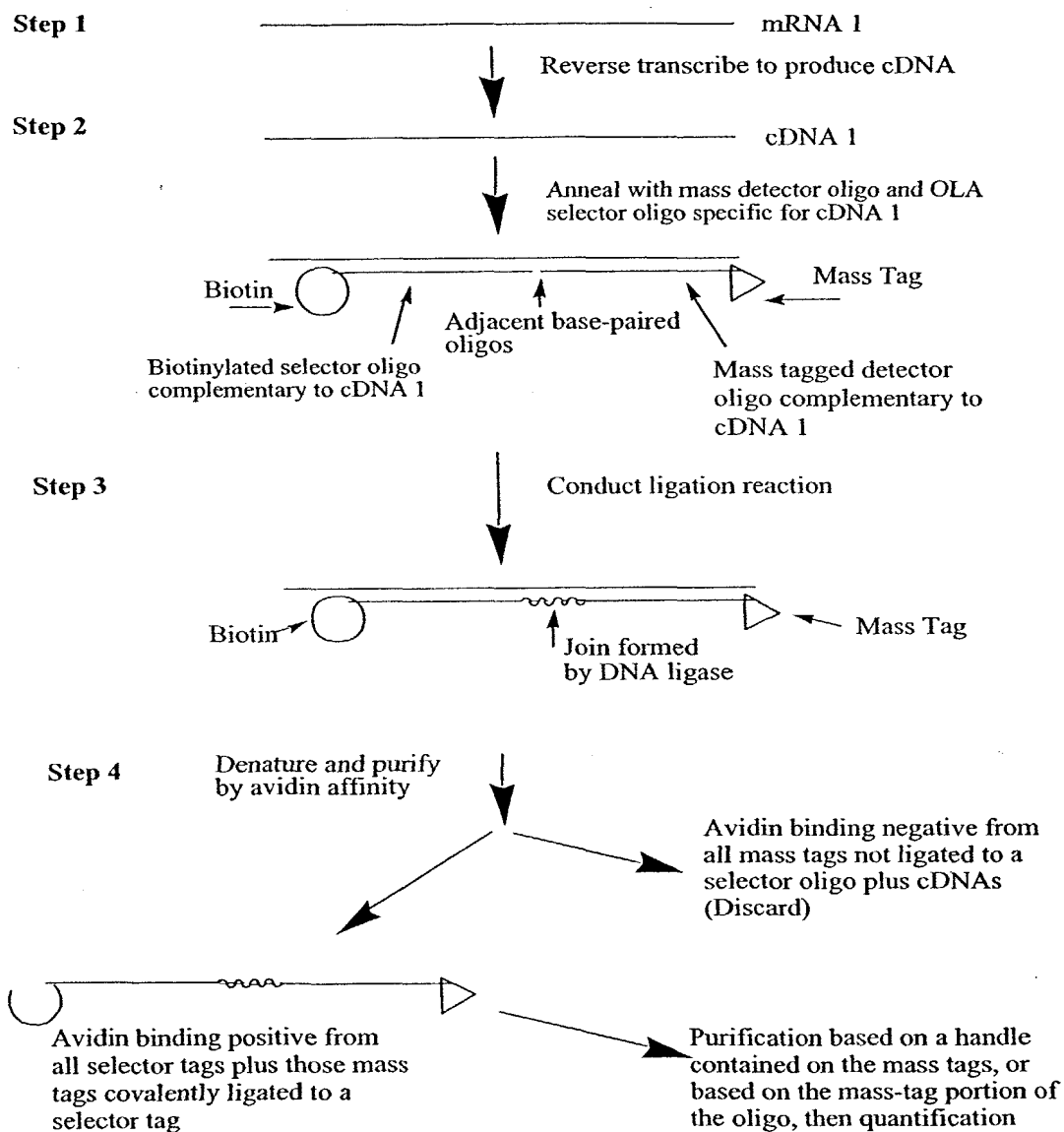
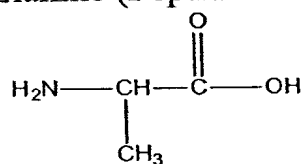


FIGURE 3

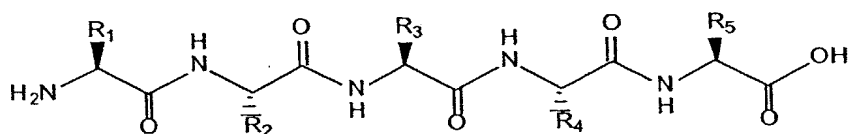
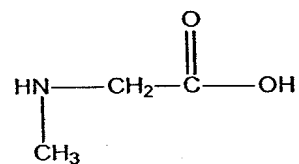
09918687 072701
T02270 48981660

alanine (Peptide monomer)

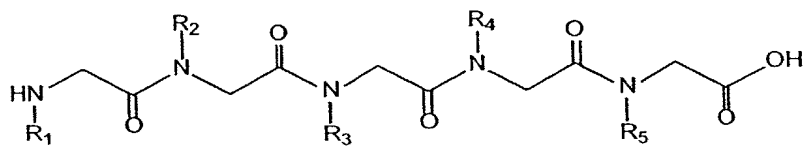


vs.

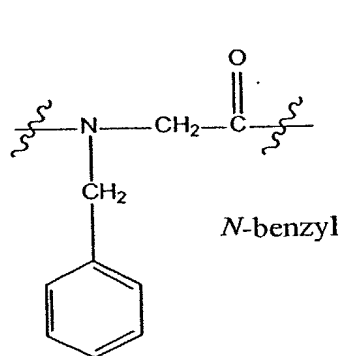
Sarcosine (Peptoid monomer)



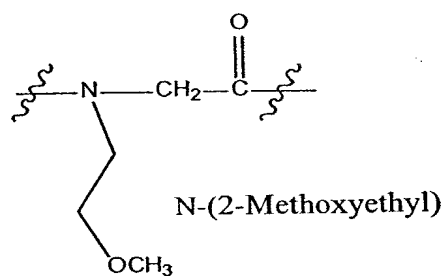
Peptide



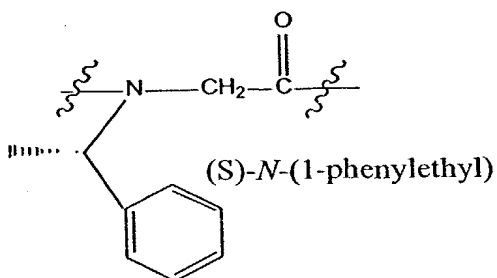
Peptoid



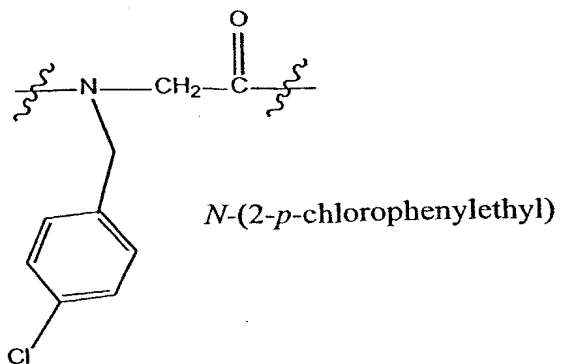
N-benzyl



N-(2-Methoxyethyl)



(*S*)-*N*-(1-phenylethyl)



N-(2-*p*-chlorophenylethyl)

FIGURE 4

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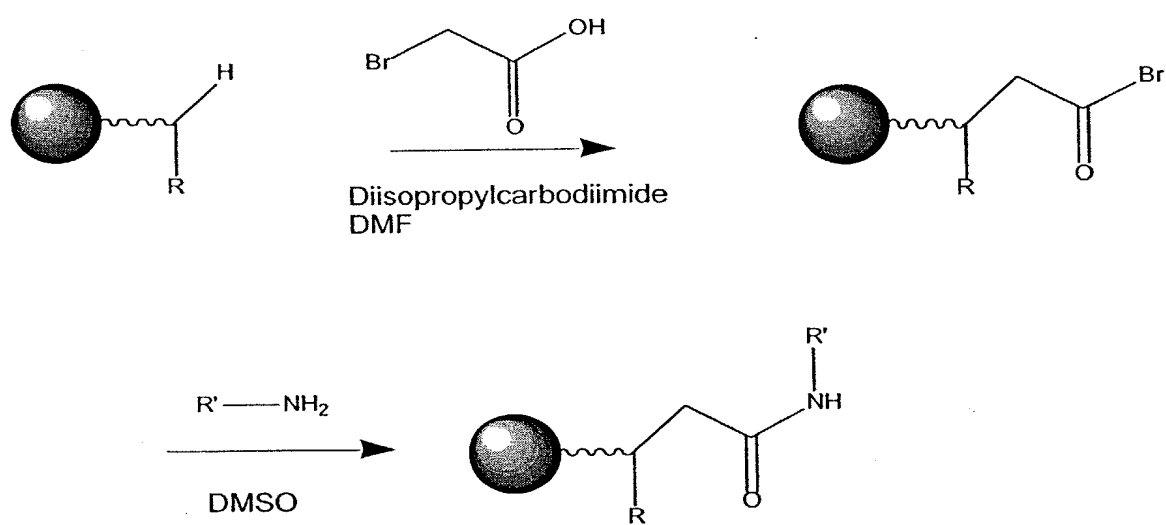
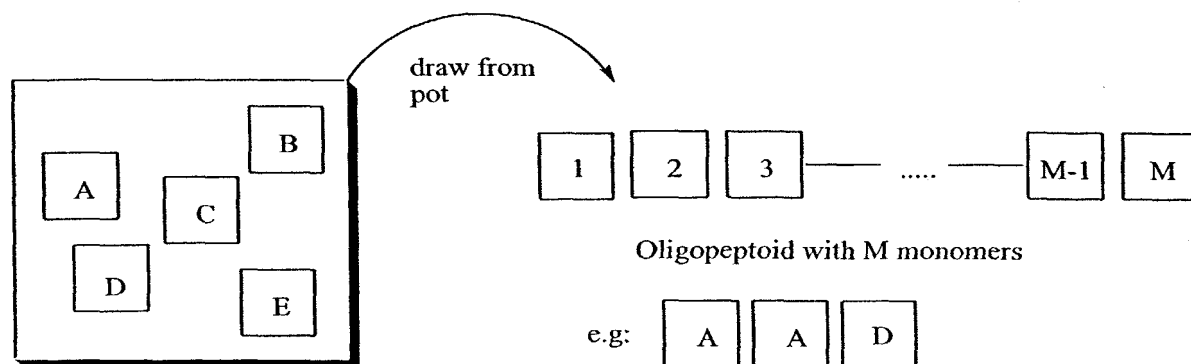


FIGURE 5

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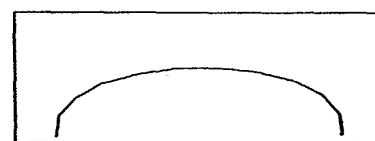


N monomers of unique mass

L = # of different peptoids with a unique combination of monomers

$$L = \binom{M+N-1}{N}$$

Example: 10 monomers, hexamer peptoids, yields 5005 combinations, or 8007 if pentamers and fewer are used too.



Mostly uniform distribution of molecular weights

Process library by removing coincidental combinations, when two unique combinations have the same mass

Also enforce other requirements, such as a minimum of X Daltons between species, or structural requirements such as at least two charged bases.

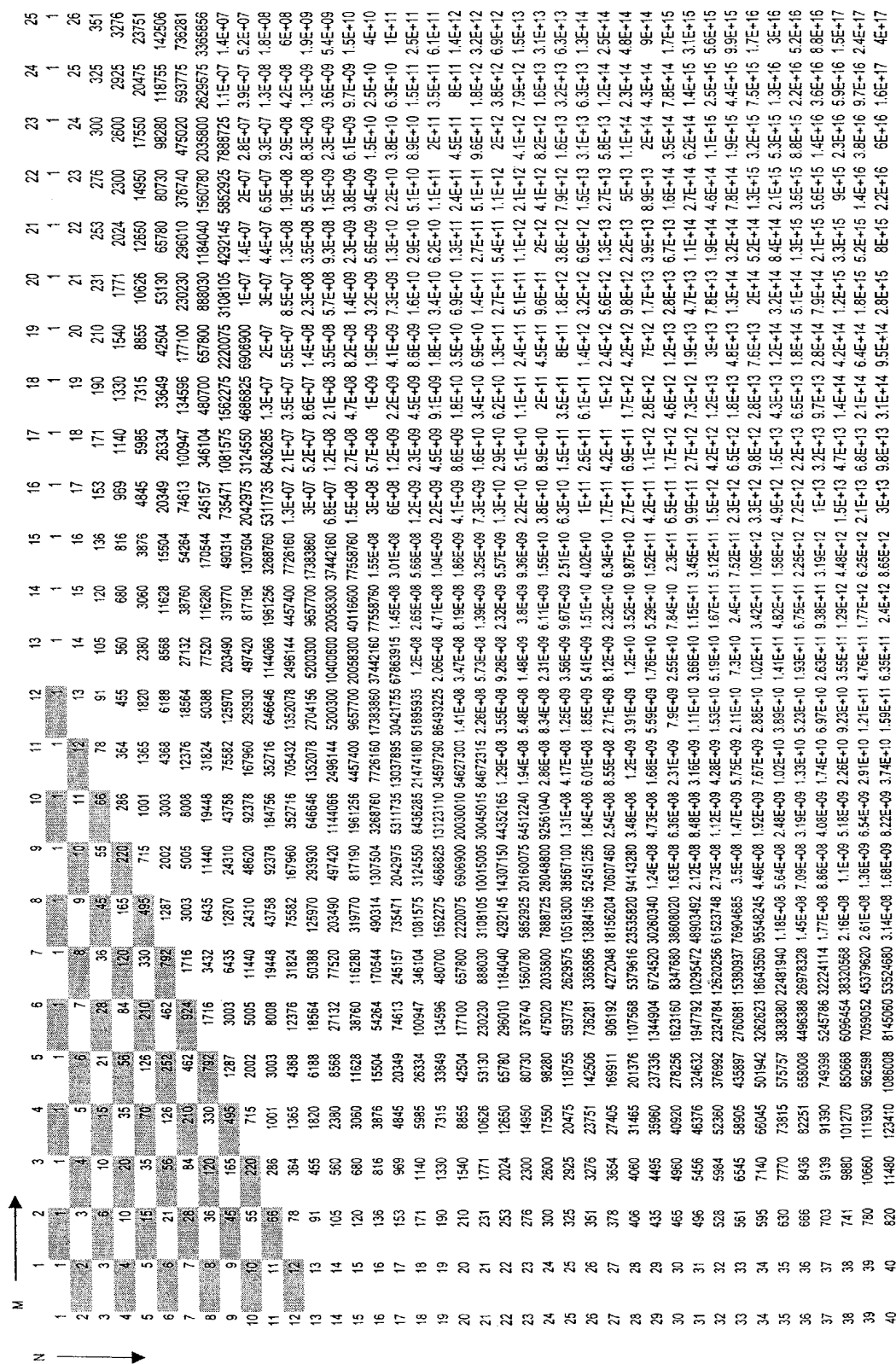


Desirable distribution of molecular weights

Assign oligo probes to tags and log, output library structure to peptoid synthesizer

FIGURE 6

Figure 7



M=length of polypeptide

N=# of monomers of unique mass

TD2240" 48987660

Figure 8A

M	N																		10	11	12
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17			
1	1	1	2	3	4	5	1	6	7	8	9	10	11	12	13	14	15	16	17	18	19
2	2	1	2	3	4	5	27	35	44	54	65	77	90	10	11	12	13	14	15	16	17
3	3	2	5	9	14	20	83	119	164	219	285	363	454	18	19	20	21	22	23	24	25
4	4	3	9	19	34	55	209	329	494	714	1000	1364	1819	26	27	28	29	30	31	32	33
5	5	4	14	34	69	125	209	329	494	714	1000	1364	1819	26	27	28	29	30	31	32	33
6	6	5	20	55	125	251	461	791	1286	2001	3002	4367	6187	34	35	36	37	38	39	40	41
7	7	6	27	83	209	461	923	1715	3002	48619	8007	12375	184755	42	43	44	45	46	47	48	49
8	8	7	35	119	329	791	1715	3431	6434	11439	1715	3431	6434	50	51	52	53	54	55	56	57
9	9	8	44	164	494	1286	3002	6434	12869	24309	3002	6434	12869	58	59	60	61	62	63	64	65
10	10	9	54	219	714	2001	5004	11439	24309	48619	5004	11439	24309	66	67	68	69	70	71	72	73
11	11	10	65	285	1000	3002	8007	19447	43757	92377	8007	19447	43757	74	75	76	77	78	79	80	81
12	12	11	77	363	1364	4367	12375	31823	75581	167959	184755	352715	705431	82	83	84	85	86	87	88	89
13	13	12	90	454	1819	6187	18563	50387	125969	293929	352715	705431	1352077	90	91	92	93	94	95	96	97
14	14	13	104	559	2379	8567	27131	77519	203489	497419	352715	705431	1352077	98	99	100	101	102	103	104	105
15	15	14	119	679	3059	11627	38759	116279	319769	817189	1961255	4457399	2496143	106	107	108	109	110	111	112	113
16	16	15	135	815	3875	15503	54263	170543	490313	1307503	3268759	7726159	17383859	114	115	116	117	118	119	120	121
17	17	16	152	968	4844	20348	74612	245156	735470	2042974	5311734	13037894	30421754	122	123	124	125	126	127	128	129
18	18	17	170	1139	5984	26333	100946	346103	1081574	3124549	8436284	21474179	51895934	130	131	132	133	134	135	136	137
19	19	18	189	1329	7314	33648	134595	480699	1562274	4686824	13123109	34597289	86493224	138	139	140	141	142	143	144	145
20	20	19	209	1539	8854	42503	177099	657799	2220074	6906899	20030009	54627299	141120524	146	147	148	149	150	151	152	153
21	21	20	230	1770	10625	53129	230229	888029	3108104	10015004	30045014	84672314	225792839	154	155	156	157	158	159	160	161
22	22	21	252	2023	12649	65779	296009	1184039	4292144	14307149	44352164	129024479	334817319	162	163	164	165	166	167	168	169
23	23	22	275	2299	14949	80729	376739	1560779	5852924	20160074	64512239	193536719	548354039	170	171	172	173	174	175	176	177
24	24	23	299	2599	17549	98279	475019	2035799	7888724	28048799	92561039	286097759	834451799	178	179	180	181	182	183	184	185
25	25	24	324	2924	20474	118754	593774	2629574	10518299	38567099	131128139	417225899	1251677699	186	187	188	189	190	191	192	193
26	26	25	350	3275	23750	142505	736280	3365855	13884155	52451255	183579395	600805295	1852482995	194	195	196	197	198	199	200	201
27	27	26	377	3653	27404	169910	906191	4272047	18156203	70607459	254186855	854992151	2707475147	202	203	204	205	206	207	208	209
28	28	27	405	4059	31464	201375	1107567	5379615	23535819	94143279	348330135	1203322287	3910797435	210	211	212	213	214	215	216	217
29	29	28	434	4494	35959	237335	1344903	6724519	30260339	124403619	472737355	1676056043	5586853479	218	219	220	221	222	223	224	225
30	30	29	464	4959	40919	278255	1623159	8347679	38608019	163011639	635745395	2311801439	7898654919	226	227	228	229	230	231	232	233
31	31	30	495	5455	46375	324631	1947791	10295471	48903491	211915131	847660527	3159461967	11058116887	234	235	236	237	238	239	240	241
32	32	31	527	5983	52359	376991	2324783	12620255	61523747	273438879	1121099407	4280561375	15338678263	242	243	244	245	246	247	248	249
33	33	32	560	6544	58904	435896	2760680	15380936	76904684	350343564	1471442972	5752004348	21090682612	250	251	252	253	254	255	256	257
34	34	33	594	7139	66044	501941	3262622	18643559	95548244	445891809	1917334782	7669339131	28760021744	258	259	260	261	262	263	264	265
35	35	34	629	7769	73814	575756	3838379	22481939	118030184	563921994	2481256777	10150595909	38910617654	266	267	268	269	270	271	272	273
36	36	35	665	8435	82250	658007	4496387	26978327	145008512	708930507	3190187285	13340783195	52251400850	274	275	276	277	278	279	280	281
37	37	36	702	9138	91389	749397	5245785	32224113	177232626	886163134	4076350420	17417133616	69668534467	282	283	284	285	286	287	288	289
38	38	37	740	9879	101269	850667	6096453	38320567	215553194	1101716329	5178066750	22595200367	92263734835	290	291	292	293	294	295	296	297
39	39	38	779	10659	111929	962597	7059051	45379619	260932814	1362649144	6540715895	29135916263	1.21E+11	298	299	300	301	302	303	304	305
40	40	39	819	11479	123409	1086007	8145059	53524679	314457494	1677106639	8217822535	37353738799	1.59E+11	306	307	308	309	310	311	312	313
		40	860	12340	135750	1221758	9366818	62891498	377348993	2054455633	10272278169	47626016969	2.06E+11	314	315	316	317	318	319	320	321

Figure 88

N	M	13	14	15	16	17	18	19	20	21	22	23	24	25
1	1	11	12	13	1	14	15	16	17	1	18	19	20	21
2	1	104	119	135	152	170	189	209	230	252	275	299	324	350
3	2	559	679	815	968	1139	1329	1539	1770	2023	2299	2599	2924	3275
4	3	2379	3059	3875	4844	5984	7314	8854	10625	12649	14949	17549	20474	23750
5	4	8567	11627	15503	20348	26333	33648	42503	53129	65779	80729	98279	118754	142505
6	5	27131	36759	54263	74612	100946	134595	177099	230229	296009	376739	475019	593774	736280
7	6	77519	116279	170543	245156	346103	480699	657799	888029	1184039	1590779	2035799	2629574	3365855
8	7	203489	319769	490313	735470	1081574	1562274	2220074	3108104	4292144	5852924	7888724	10518299	13884155
9	8	497419	817189	1307503	2042974	3124549	4666824	6906899	10015004	14307149	20160074	28046799	38567099	52451255
10	9	1144065	1961255	3268759	5311734	8436284	13123109	20030009	30045014	44352164	64512239	92561039	131128139	183579395
11	10	2496143	4457399	7726159	13037894	21474179	34597289	54627299	84672314	129024479	193536719	286097759	417225899	600805295
12	11	5200299	9657899	17383859	30421754	51895934	86493224	141120524	225792839	354817319	548354039	834451799	1251677699	1852482995
13	12	10400599	20058299	37442159	67863914	119759849	206253074	347373599	573166439	927983759	1476337799	2310789599	3562467299	5414502935
14	13	20058299	40116599	77558759	145422674	265182524	471435599	818809199	1391975639	2319959399	3796297199	6107086799	9669554099	15084504395
15	14	37442159	77558759	155117519	300540194	565722719	1037158319	1855967519	3247943159	5567902559	9364199759	15471286559	25140840559	40225345055
16	15	67863914	145422674	300540194	601080389	1166803109	2203961429	405928949	7307872109	12875774699	22239974429	37711260989	62852101649	103077E+11
17	16	119759849	265182524	565722719	1166803109	2203961429	405928949	8597496599	15905368709	28781143379	5102117809	88732378799	151584E+11	25466E+11
18	17	206253074	471435599	1037158319	2203961429	405928949	8597496599	17672631899	33578000609	62359143969	11338E+11	202113E+11	353697E+11	608359E+11
19	18	347373599	818809199	1855967519	405928949	8597496599	17672631899	35345263799	68923284409	131282E+11	244663E+11	446775E+11	800472E+11	140883E+12
20	19	573166439	1391975639	3247943159	7307872109	15905368709	28781143379	5102117809	137847E+11	289129E+11	513792E+11	90667E+11	176104E+12	316987E+12
21	20	927983759	2319959399	5567902559	12875774699	26781143379	62359143969	131282E+11	269129E+11	538258E+11	106205E+12	201262E+12	377366E+12	694353E+12
22	21	1476337799	3796297199	9364199759	22239974429	5102117809	11338E+11	244663E+11	513792E+11	105205E+12	21041E+12	411672E+12	789037E+12	148339E+13
23	22	231769599	6107086799	15471286559	37711260989	88732378799	202113E+11	446775E+11	90667E+11	201262E+12	411672E+12	823343E+12	161238E+13	309577E+13
24	23	3562467299	9669554099	25140840559	62852101649	151584E+11	353697E+11	800472E+11	176104E+12	377366E+12	789037E+12	161238E+13	322476E+13	632053E+13
25	24	5414502935	15084504395	40225345055	103077E+11	254662E+11	608359E+11	140883E+12	316987E+12	694353E+12	148339E+13	309577E+13	632053E+13	12641E+14
26	25	8122425443	23206929839	63432274895	16651E+11	421172E+11	102953E+12	243836E+12	560823E+12	125518E+13	273857E+13	583434E+13	121549E+14	247659E+14
27	26	12033222879	35240152719	96672427615	265182E+11	686354E+11	171598E+12	415425E+12	976248E+12	223142E+13	496999E+13	106043E+14	229592E+14	477551E+14
28	27	17620076359	52860229079	151533E+11	416719E+11	110307E+12	281895E+12	69732E+12	167357E+13	390499E+13	887498E+13	196793E+14	426385E+14	903939E+14
29	28	25518731279	78378960359	229912E+11	646628E+11	17497E+12	456865E+12	115418E+13	282775E+13	673274E+13	156077E+14	35287E+14	779255E+14	168319E+15
30	29	36576848167	114956E+11	344867E+11	991494E+11	274119E+12	730984E+12	188517E+13	471292E+13	114457E+14	270534E+14	623404E+14	140266E+15	308585E+15
31	30	51915526431	166871E+11	511739E+11	150323E+12	424442E+12	115543E+13	304059E+13	75352E+13	191992E+14	462526E+14	108593E+15	248859E+15	557444E+15
32	31	7306209044	239879E+11	751616E+11	225485E+12	649927E+12	180535E+13	484595E+13	125995E+14	317986E+14	780512E+14	186644E+15	435503E+15	982947E+15
33	32	10766E+11	34164E+11	109326E+12	33481E+12	984738E+12	279009E+13	763604E+13	202355E+14	520341E+14	130085E+15	31673E+15	752233E+15	174519E+16
34	33	140677E+11	482321E+11	157558E+12	492369E+12	147711E+13	42672E+13	119032E+14	321387E+14	841729E+14	214258E+15	530888E+15	128322E+16	30284E+16
35	34	192928E+11	675249E+11	225083E+12	717452E+12	219456E+13	646178E+13	18365E+14	506037E+14	134677E+15	348935E+15	879923E+15	216314E+16	519154E+16
36	35	262597E+11	937846E+11	318868E+12	103632E+13	323066E+13	969263E+13	280576E+14	785614E+14	213238E+15	562173E+15	14421E+16	360524E+16	879679E+16
37	36	354861E+11	129271E+12	448138E+12	148448E+13	471534E+13	14409E+14	424656E+14	121027E+15	334265E+15	896438E+15	233853E+16	594377E+16	147408E+17
38	37	47626E+11	176997E+12	625035E+12	210949E+13	682483E+13	212328E+14	63694E+14	184725E+15	51899E+15	141543E+16	375396E+16	69773E+16	240383E+17
39	38	635014E+11	240398E+12	865433E+12	297493E+13	979975E+13	310328E+14	947309E+14	279456E+15	798447E+16	21387E+16	596784E+16	156656E+17	401039E+17
40	39	841393E+11	324537E+12	118997E+13	41649E+13	13646E+14	449972E+14	139728E+15	419184E+15	121763E+16	343151E+16	939934E+16	250649E+17	651689E+17

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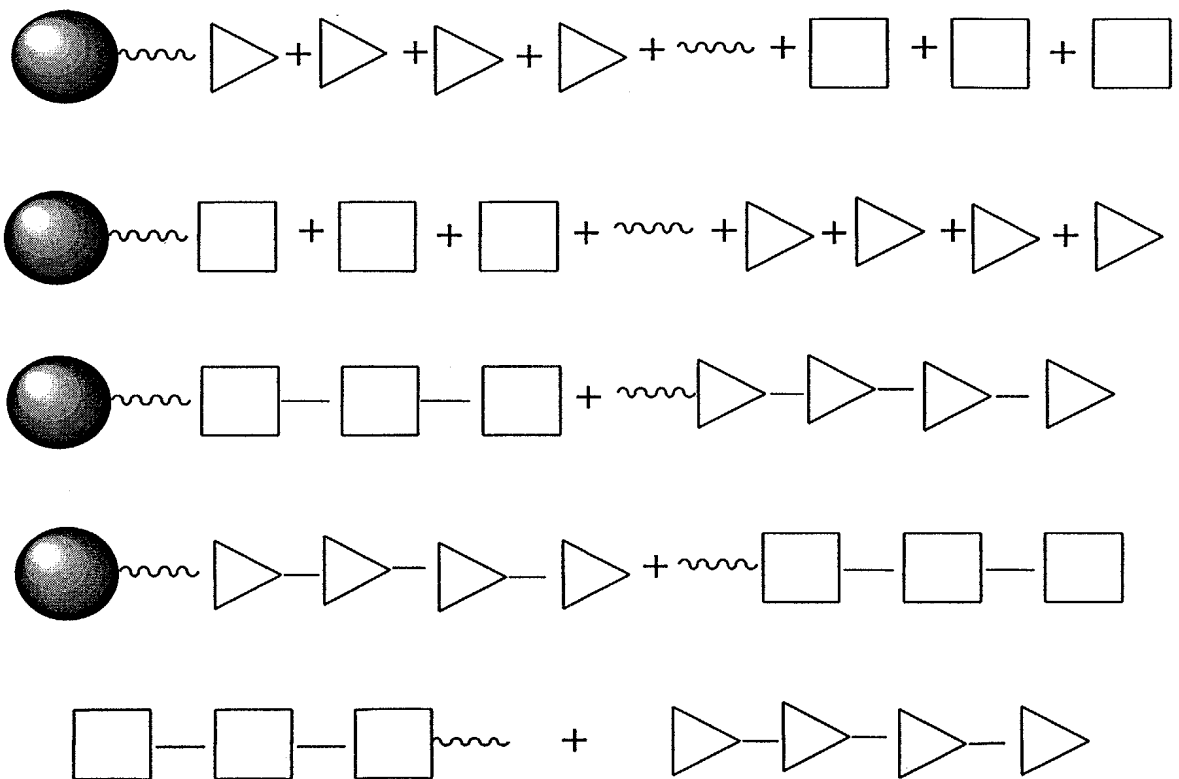
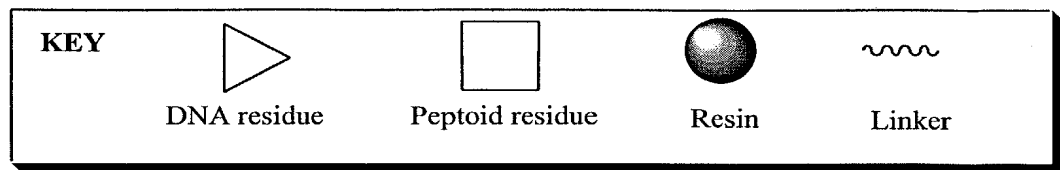
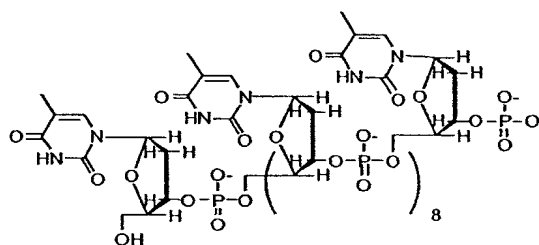
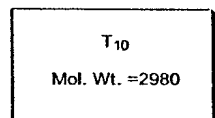


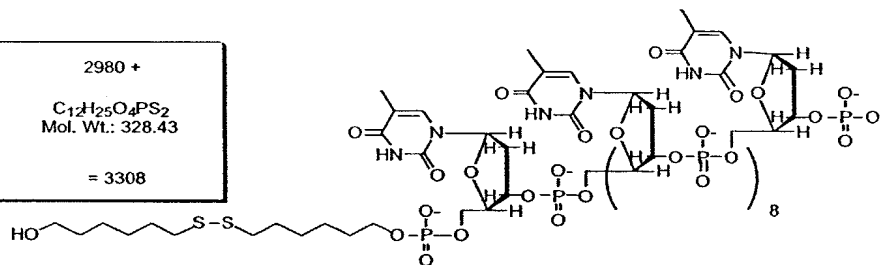
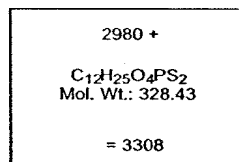
FIGURE 9

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N1



N2



N3

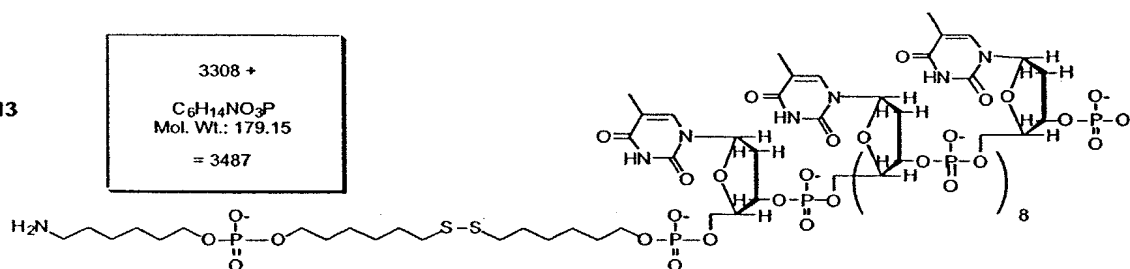
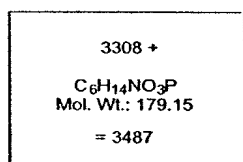


FIGURE 10

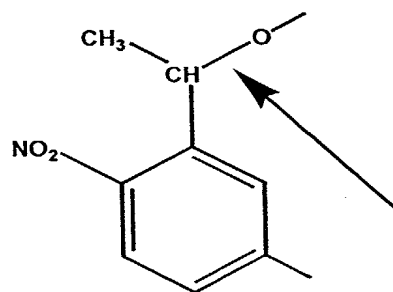


FIGURE 11A

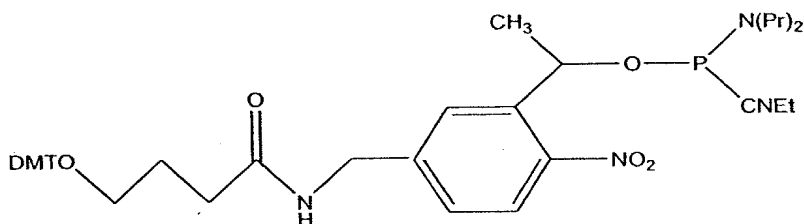


FIGURE 11B

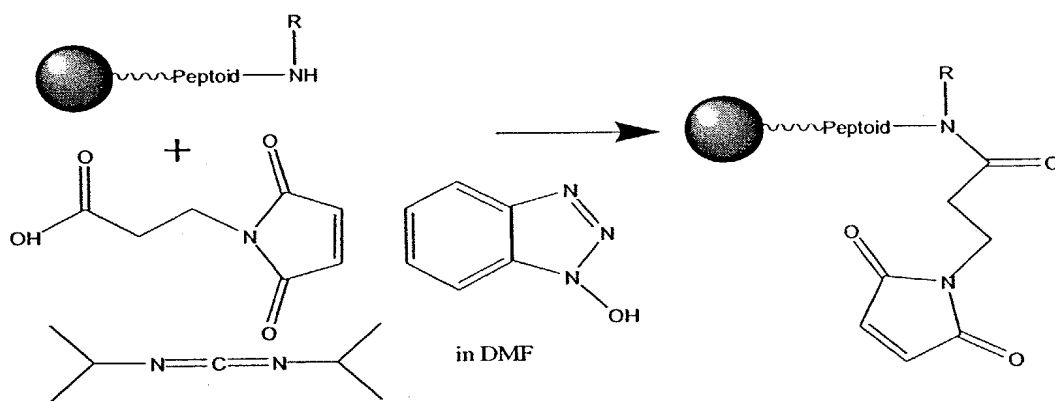


FIGURE 11C

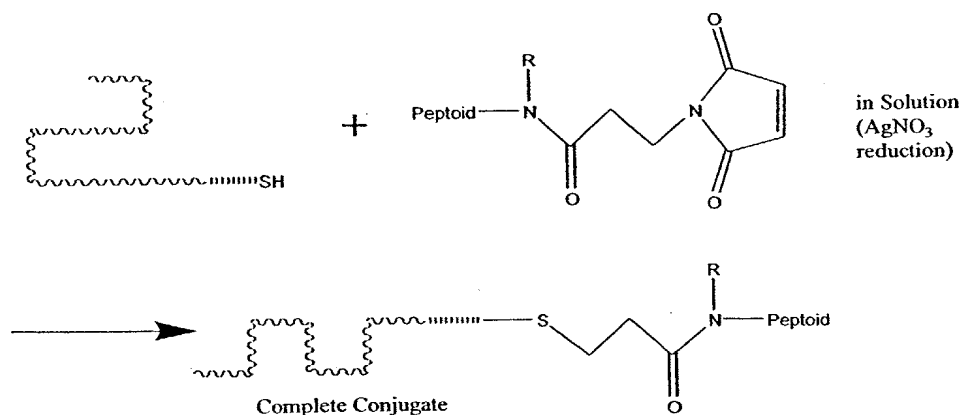


FIGURE 11D

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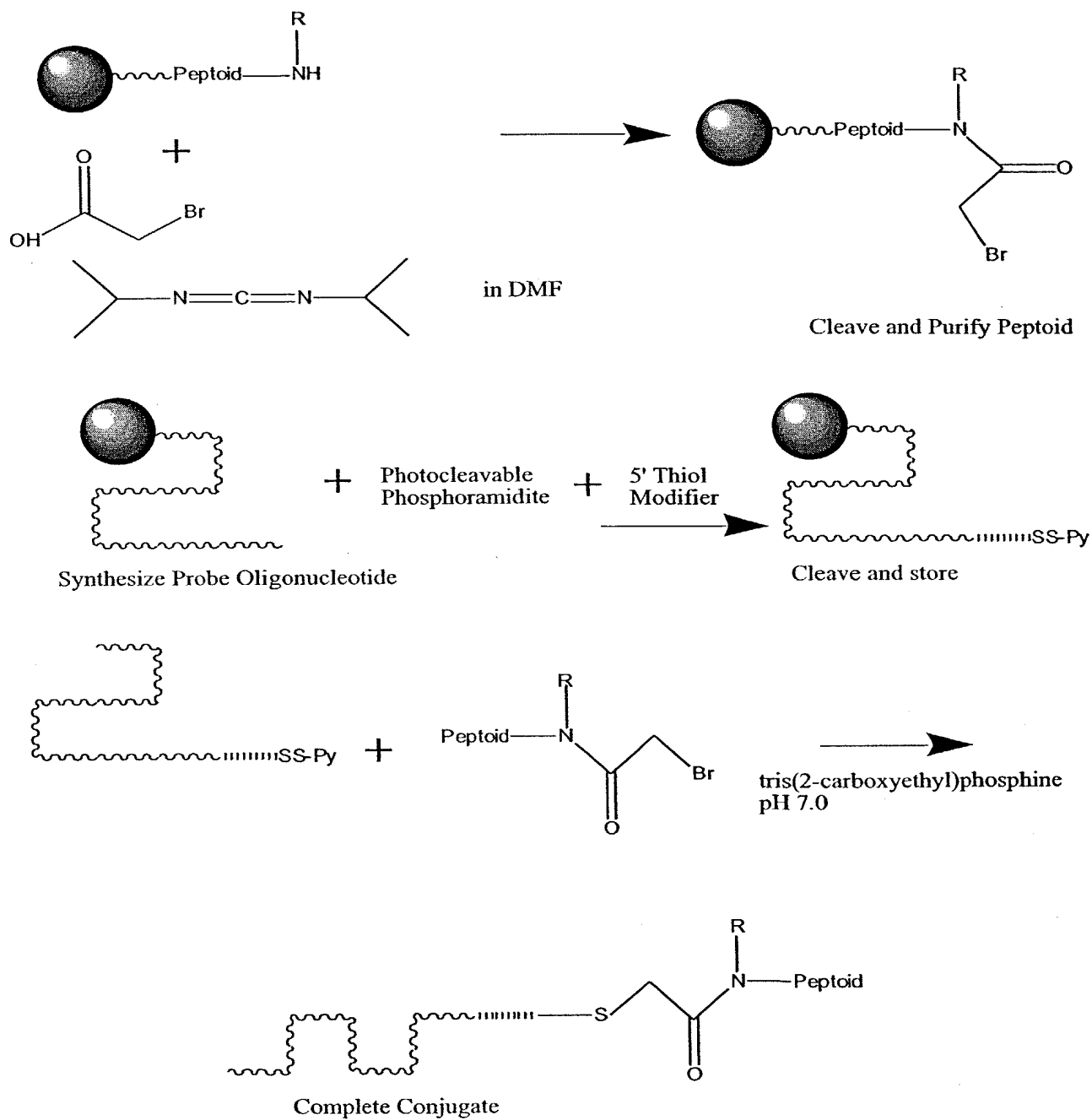
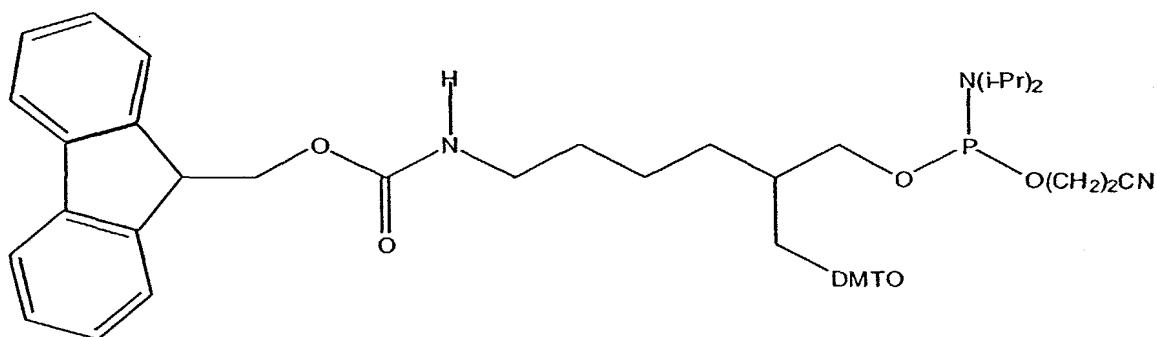


FIGURE 11E



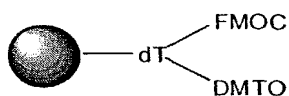
Clontech "Uni-Link AminoModifier" Branched Phosphoramidite

Method

1. Obtain Oligonucleotide Resin with dT base



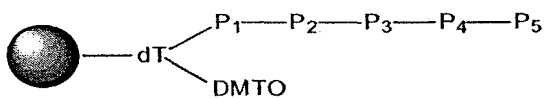
2. Add Branched Phosphoramidite



3. Transfer to Peptoid Synthesizer

4. Deprotect Fmoc

5. Add Peptoid



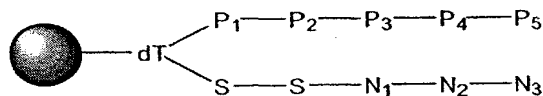
6. Protect Terminus

7. Return to ODN Synthesizer

8. Deprotect DMTO

9. Add cleavable units (Disulfide or Photocleavable)

10. Synthesize ODN



11. Deprotect and Cleave Completed Unit

FIGURE 12

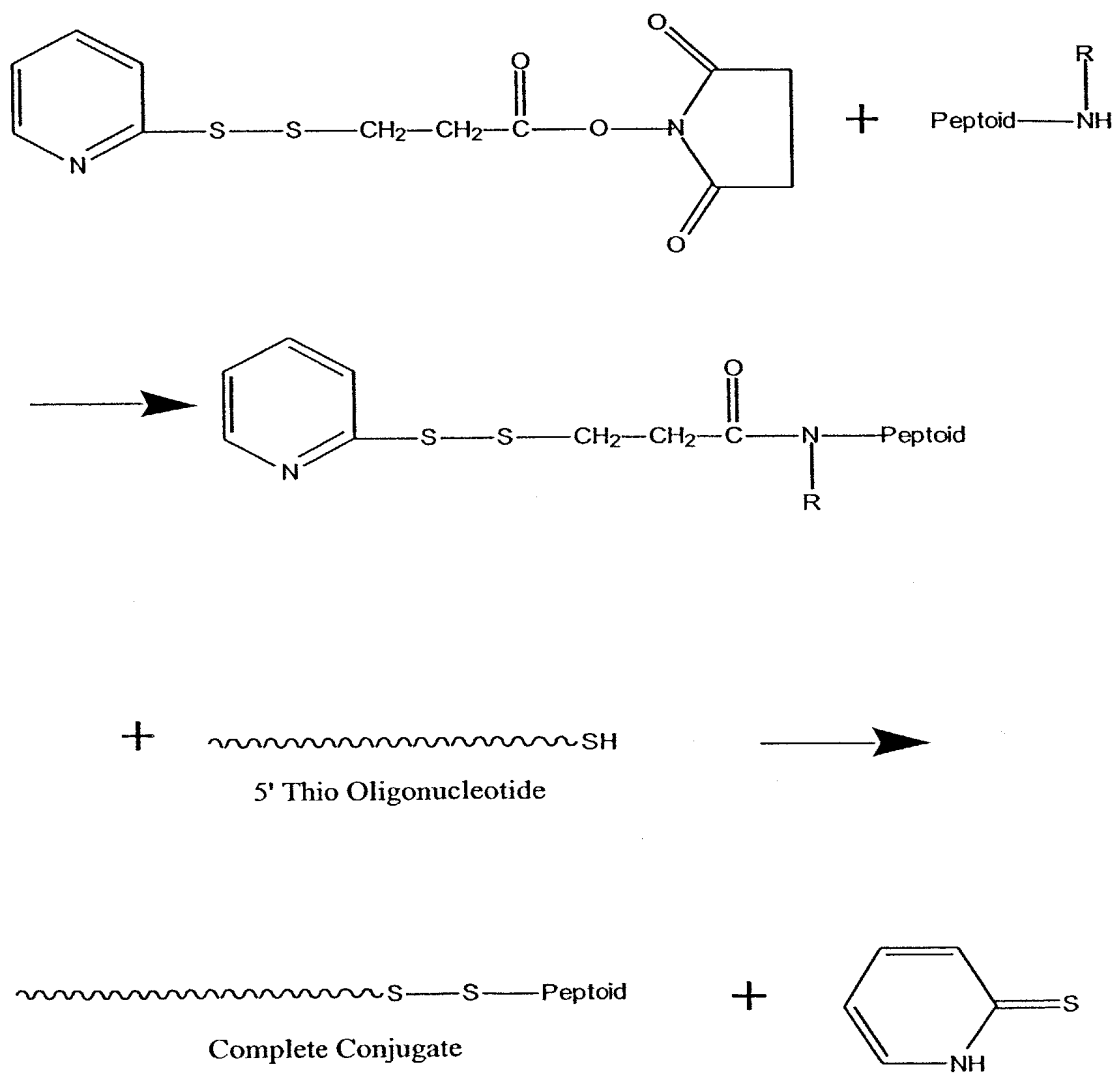


FIGURE 13

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10/22/07 1898T660

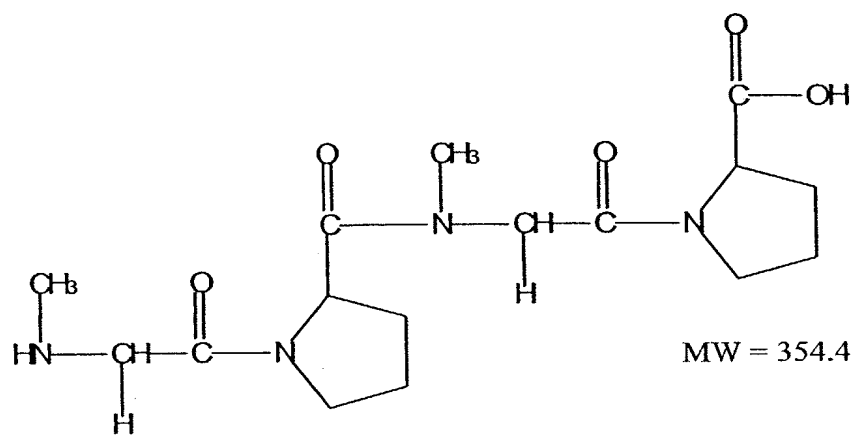


FIGURE 14

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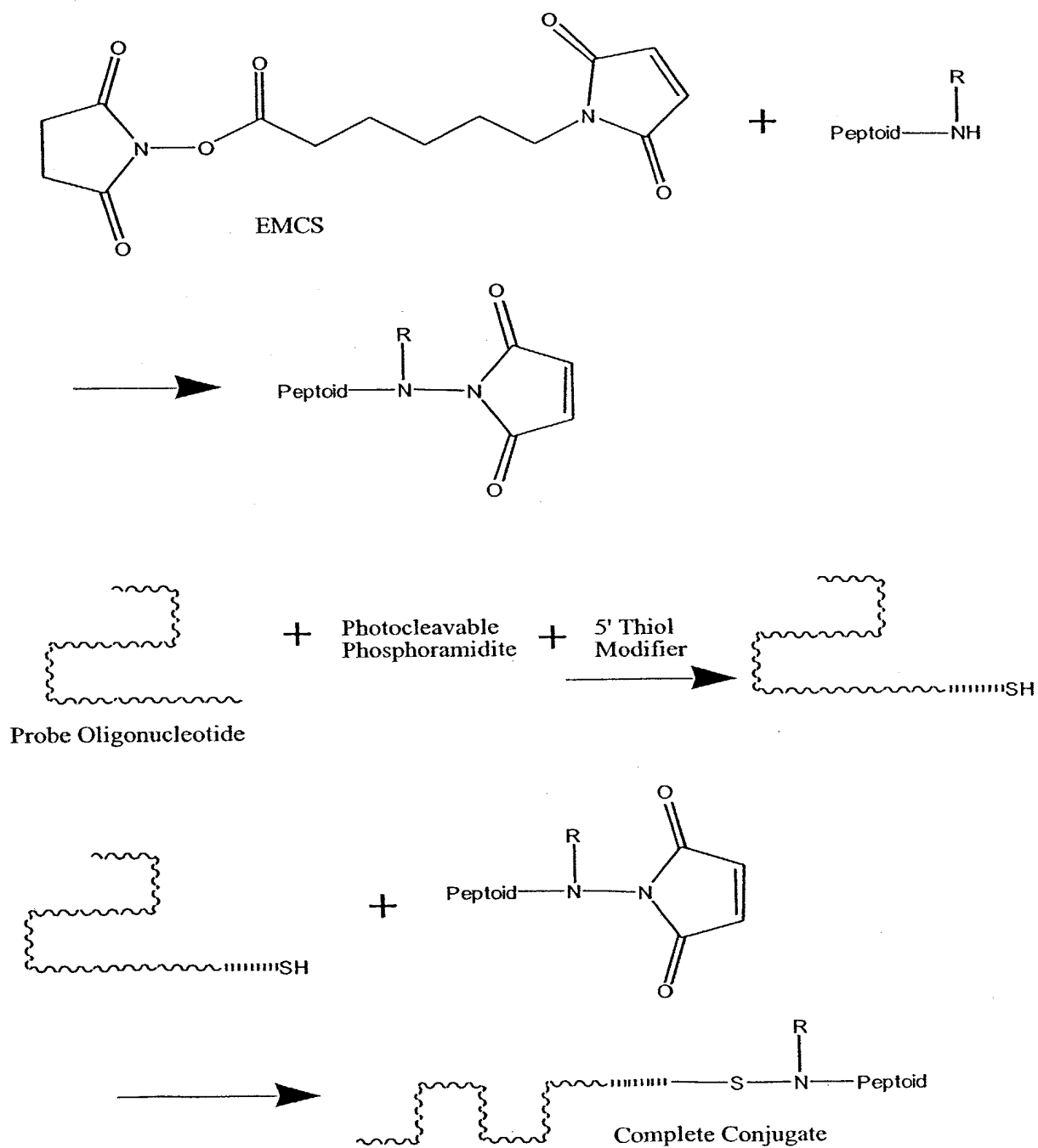


FIGURE 15

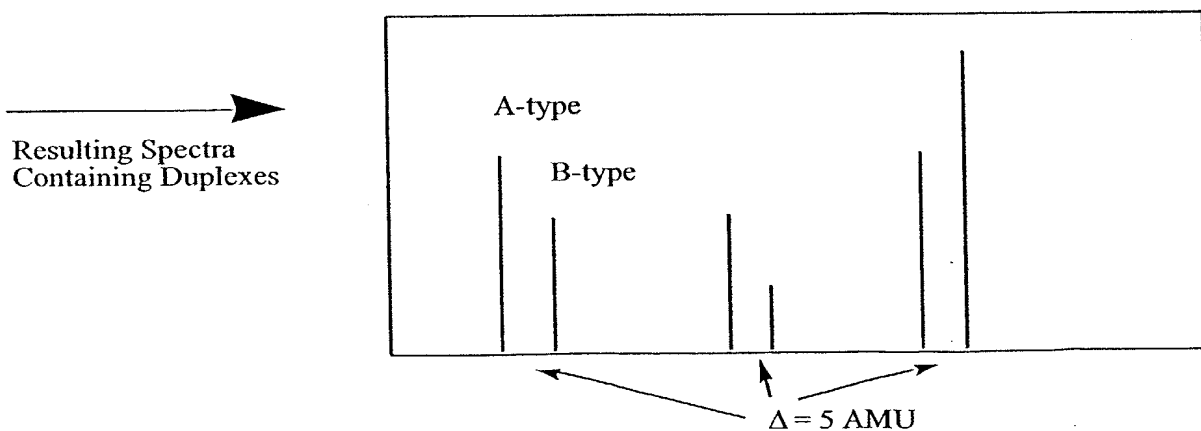
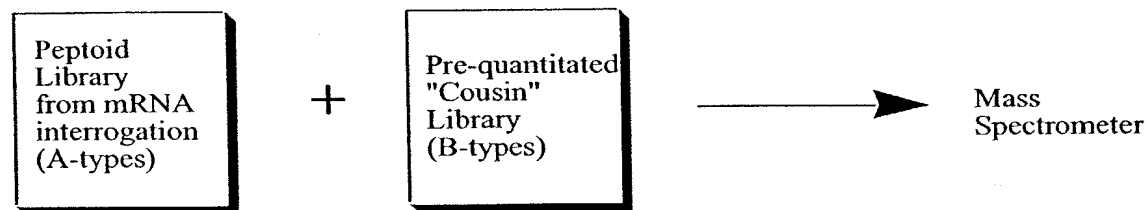
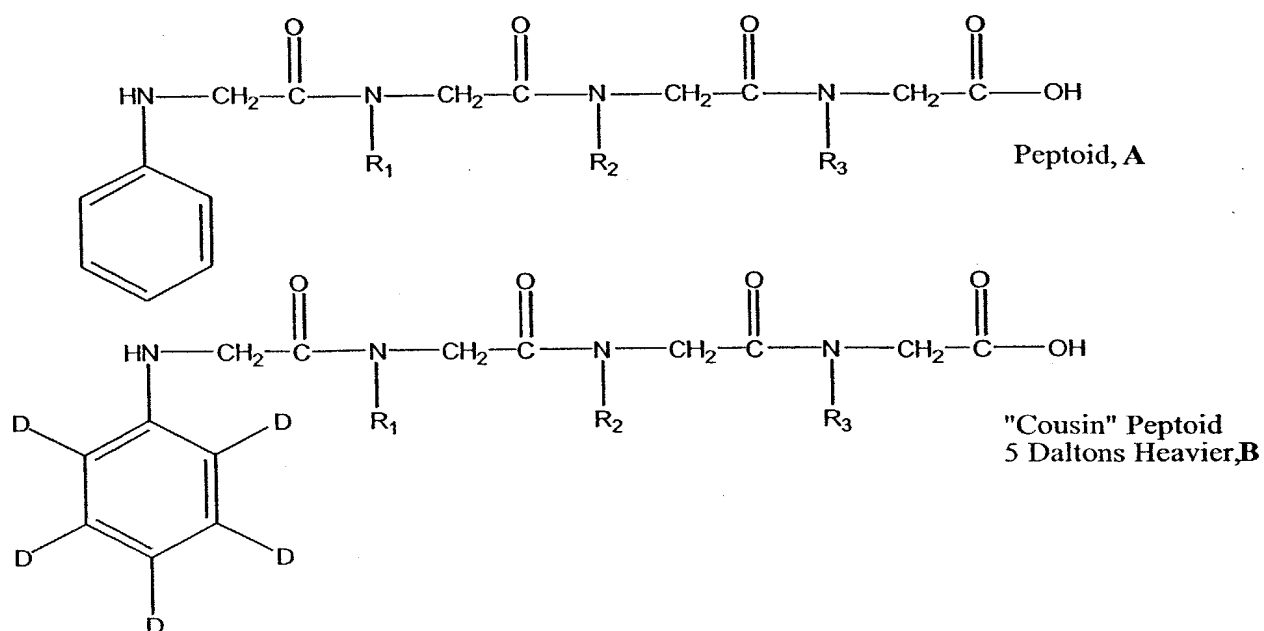


FIGURE 16

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T02220 18981660

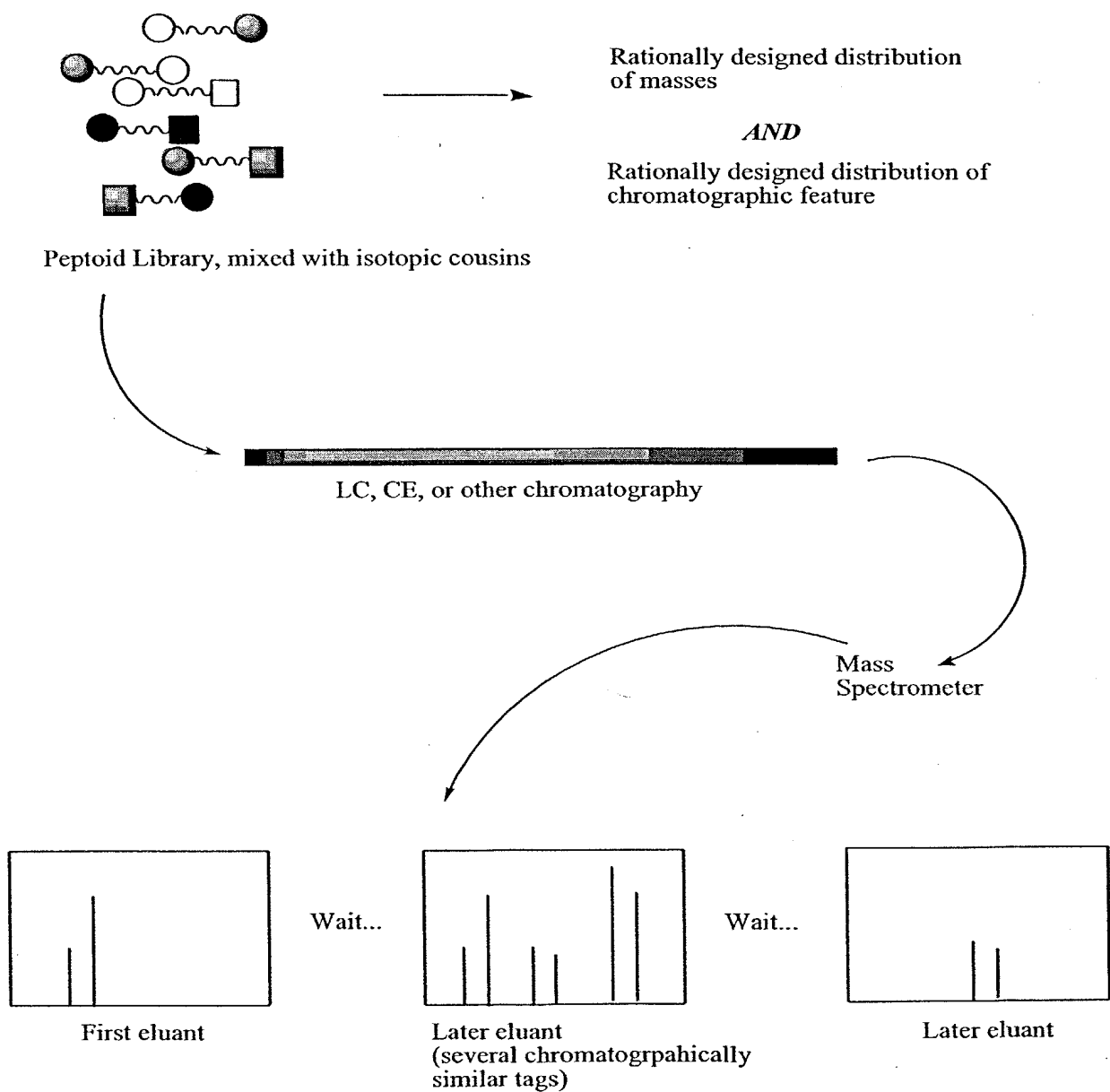
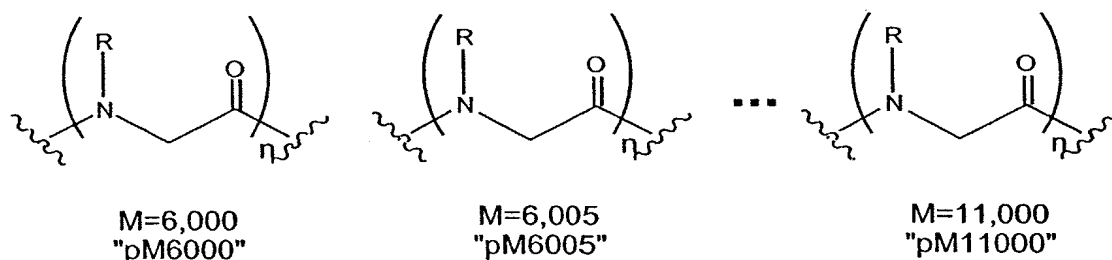


FIGURE 18

- 1) Synthesize and purify 1000 different peptoid oligomer mass tags, of mass 6,000 to 11,000 Daltons.



This will be performed by a robotic synthesizer on solid phase, with oligomer lengths of up to 40 residues. Molecular weights per residue will be 150-300 Daltons.

- 2) Synthesize and purify 16,000 different DNA oligos, complementary to the mRNA specie to be detected. Create 16 libraries of 1,000 oligos each.

AA(NNNNNNNN)₁, AA(NNNNNNNN)₂, ..., AA(NNNNNNNN)_{1,000}

AC(NNNNNNNN)₁, AC(NNNNNNNN)₂, ..., AC(NNNNNNNN)_{1,000}

.....

TT(NNNNNNNN)₁, TT(NNNNNNNN)₂, ..., TT(NNNNNNNN)_{1,000}

- 3) Specifically conjugate oligos in each library to a corresponding peptoid mass tag.

AA(NNNNNNNN)₁/pM6000, AA(NNNNNNNN)₂/pM6005, ..., AA(NNNNNNNN)_{1,000}/pM11000

AC(NNNNNNNN)₁/pM6000, AC(NNNNNNNN)₂/pM6005, ..., AC(NNNNNNNN)_{1,000}/pM11000

.....

TT(NNNNNNNN)₁/pM6000, TT(NNNNNNNN)₂/pM6005, ..., TT(NNNNNNNN)_{1,000}/pM11000

- 4) Purify DNA/peptoid mass tag products and combine library elements into 16 pools.

FIGURE 19

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Mass-tagging on a chip: How to measure levels of 16,000 mRNA species in solution

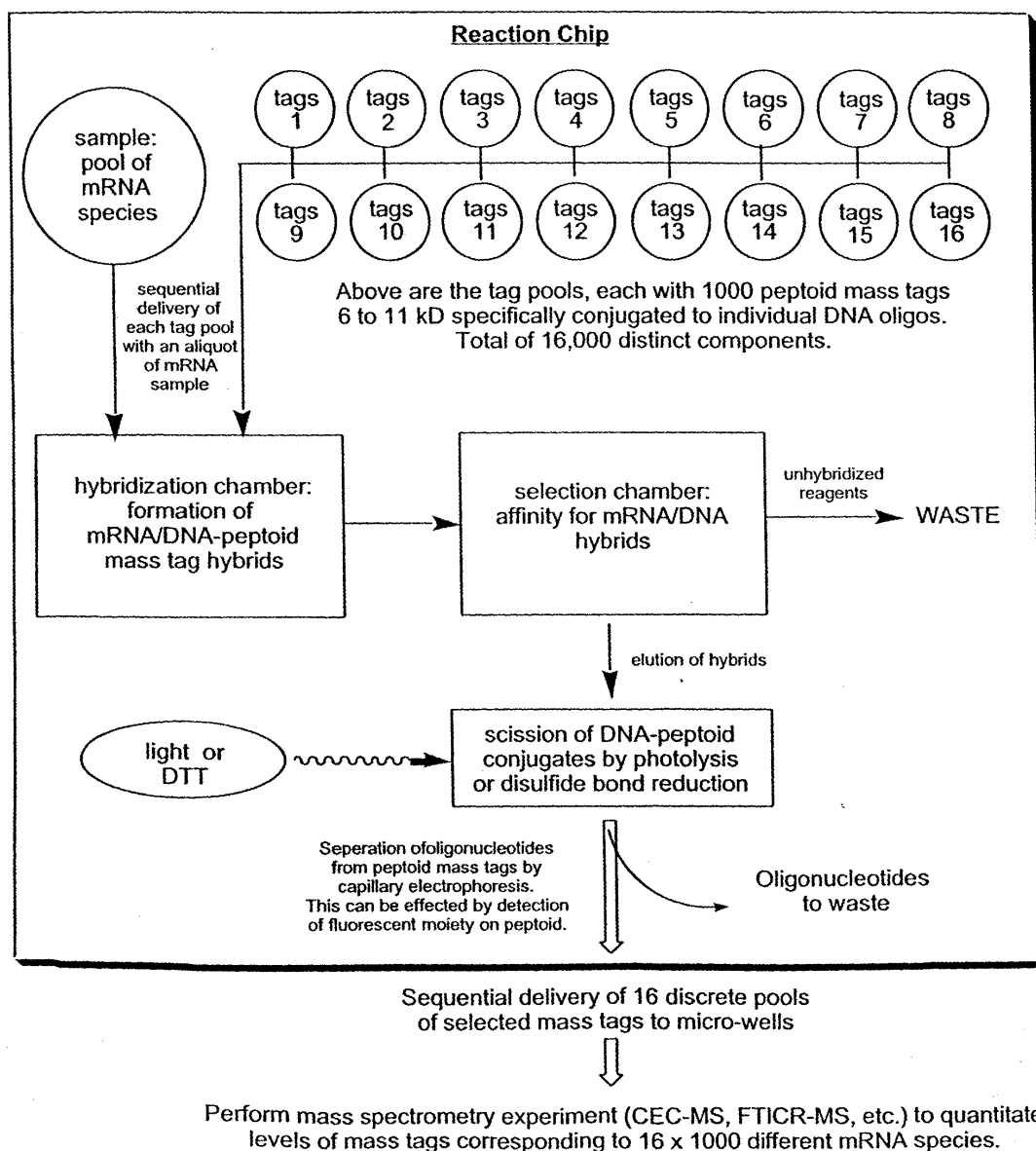


FIGURE 20

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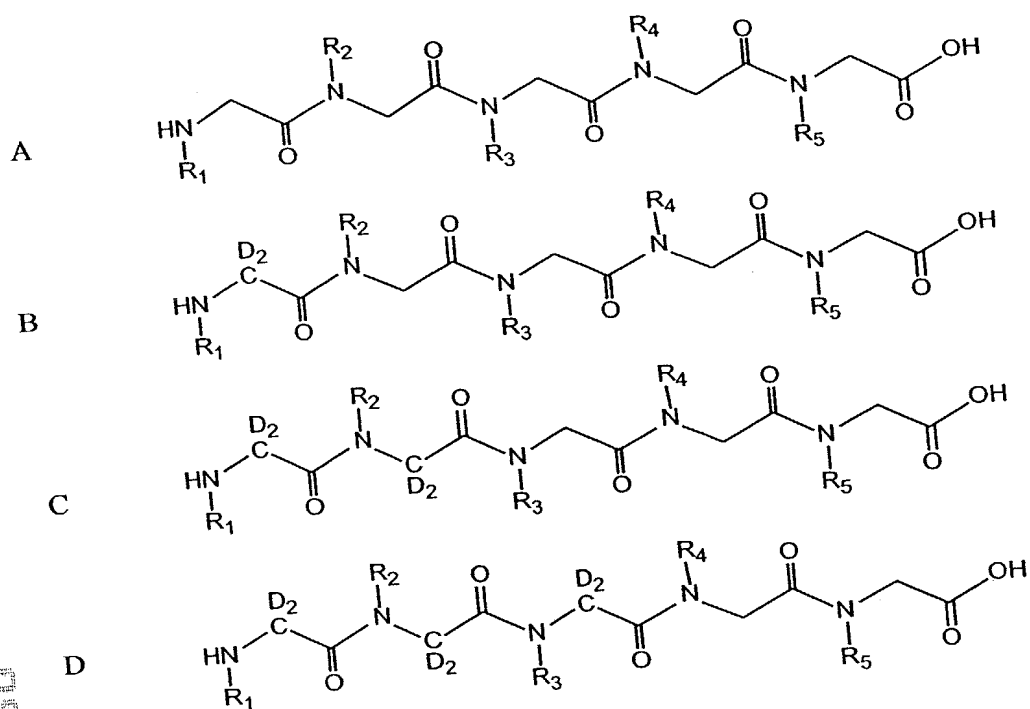


FIGURE 21

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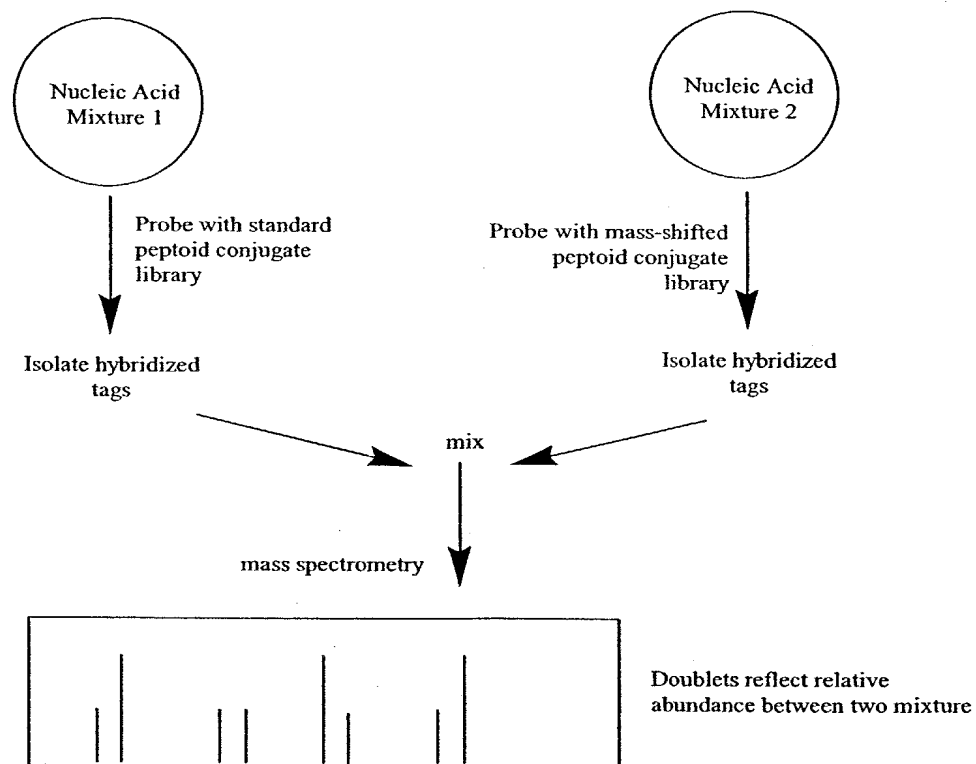


FIGURE 22

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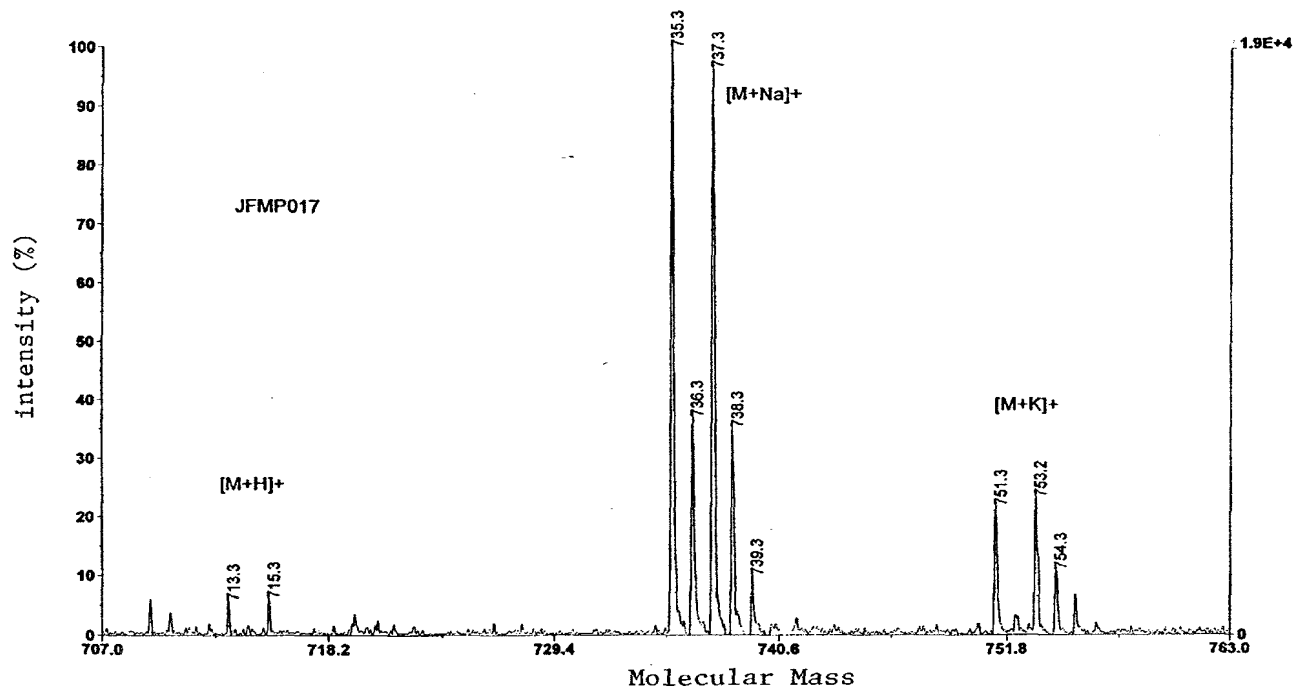


FIGURE 23